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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/525,883

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Ursula Giesen

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EXAMINER

WHITE, DENNIS MICHAEL

ART UNIT

PAPER NUMBER

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/525,883	<b>Applicant(s)</b> GIESEN ET AL.	
	<b>Examiner</b> DENNIS M. WHITE	<b>Art Unit</b> 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-23 and 25-29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-17, 21-23 and 25-29 is/are rejected.
- 7) ☒ Claim(s) 18-20 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

1. Amendments filed on 01/28/2009. Claims 1, 23, 25-28 are amended. Claim 24 is cancelled. Claim 29 is new. Currently claims 1-23, 25-29 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. Claims 1, 3-4, 7, 9-17, 21-22, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fiaccabrino et al (1997 International Conference on Solid-state Sensors and Actuators, Chicago, June 16-19, 1997, Pg. 171-174) in view of Rubinstein et al (J. Am. Chem. SOC. 1981, 103, 512-516).

Regarding claim 1, 3-4, 7, 9-17, 21-22, and 27, Fiaccabrino et al teach a method of electrogenerated chemiluminescence (ECL) from a solution of  $\text{Ru}(\text{bpy})_3^{2+}$  comprising ruthenium(II) tris(2,2-bipyridyl) ("homogenous test") generated at an interdigitated microelectrode array (IDA) and detected with an onchip integrated silicon photodiode is reported. Chemiluminescence was generated at one of the cells when applying the appropriate redox potentials to the interdigitated anode and cathode. The electrode potentials were independently controlled by an in-house built bipotentiostat. The cathode (generator) was either cycled or pulsed from 1.65 ("oxidizing a metal complex" "oxidized electrochemically" "oxidation takes place by applying an anodic potential of at least +1.2V relative to an Ag/AgCl reference electrode") to -1.45 V ("reducing the metal complex", since the reaction is carried out in water the

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production of hydrogen is inherent because of the -1.45V, "nascent hydrogen is generated in the direct vicinity of the metal complex" "reduction is separated in time from the oxidation" "nascent hydrogen is generated electrochemically" "electrochemical generation is carried out by applying a voltage of  $\leq -1.0V$  relative to an Ag/AgCl reference electrode"; regarding claim 17, "chemically" is sufficiently broad to read on the conversion of water to hydrogen) and the anode (collector) was kept at a constant potential value of 1.65 V. The dielectric layer isolating the IDA from the photodiode protects the semiconductor device from being exposed to the analyte ("contacting a sample containing an analyte with a detecting reagent which carries the metal complex that is capable of chemiluminescing") (Pg. 171 col.1 para. 2 and Pg. 172 col. 1 para. 4).

Fiaccabrino et al are silent about the oxidizing and reducing ("generation of nascent hydrogen") step take place in separate reaction chambers, the metal complex is oxidized chemically by PbO<sub>2</sub>, permanganate, Ce<sup>4+</sup> compounds or/and peroxodisulfate.

Rubenstein et al teach an aqueous system for electrogenerated chemiluminescence (ecl) based on the reaction of electrogenerated Ru(bpy)<sub>3</sub><sup>2+</sup> with strong reductants produced as intermediates in the oxidation of oxalate ion is described. Chemiluminescence was also observed with other organic acids (pyruvic, malonic, lactic), when the intermediates produced on their oxidation by Ce<sup>4+</sup> reacted with Ru(bpy)<sub>3</sub><sup>2+</sup>. Another possibility is to make use of a chemical oxidizing agent in a light-generating device. This was done with the flow system shown in Figure 4. The solution flowing in a closed circuit was 1.0 mM

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$\text{Ru}(\text{bpy})_3^{2+}$  in 0.1 M  $\text{H}_2\text{SO}_4$ , and the solids in the two compartments were gently stirred. The slightly soluble  $\text{BaC}_2\text{O}_4$  in compartment a provides a constant supply of oxalate ions to compartment b, where they react with  $\text{Ru}(\text{bpy})_3^{2+}$  that was produced by oxidation of  $\text{Ru}(\text{bpy})_3^{2+}$  by  $\text{PbO}_2$ . As a result, one observes a constant light emission from compartment b (Fig. 4 below).

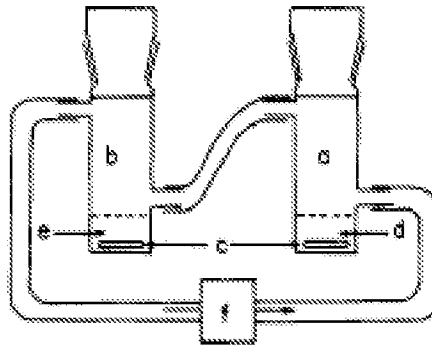


Figure 4. Flow system for continuous light generation: a and b, glass compartments; c, magnetic stirrer; d, solid  $\text{BaC}_2\text{O}_4$ ; e, solid  $\text{PbO}_2$ ; f, peristaltic pump.

It is desirable to keep the oxidation and reduction chambers separate in order to make sure the oxidizing agents do not react with the reducing agents and the metals are completely oxidized before being reduced. It is well known to oxidize the  $\text{Ru}(\text{bpy})_3^{2+}$  by  $\text{PbO}_2$ .

Therefore it would have been obvious to one of ordinary skill in the art to modify the method and device of Fiaccabrino with the separate oxidation and reduction chambers of Rubenstein in order to make sure the oxidizing agents do not react with the reducing agents and the metals are completely oxidized before being reduced.

Simple substitution of one known element for another to obtain predictable results is held to be obvious. Therefore, it would have been obvious to one of

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ordinary skill in the art to substitute the electrochemical oxidation of Fiaccabrino with the oxidation by  $\text{PbO}_2$  of Rubenstein because  $\text{PbO}_2$  is a well known oxidizing agent for  $\text{Ru}(\text{bpy})_3^{2+}$  in electrogenerated chemiluminescence.

4. Claims 2, 5-6, 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fiaccabrino et al in view of Rubinstein et al and further in view of Josel et al (USP 5,958,783).

Fiaccabrino/Rubenstein teach the limitations of claim 1 as per above.

Regarding claim 2, 5-6, 8, Fiaccabrino/Rubenstein teach the metal complex comprises  $\text{Ru(II)(bpy)}_3$ . Fiaccabrino/Rubenstein are silent about a linker bound to one of the ligands, the metal complex comprises at least one hydrophilic group or/and a charge carrier, the metal complex used as a conjugate with a detection reagent for the analyte, and the detection is carried out as a heterogenous test.

Josel et al (USP 5,958,783) teach metal complexes such as  $\text{Ru(II)(bpy)}_3\text{-X}$ , where the X is a charged linkers bound to one of the bipyridiyl ligands (col. 1 line 55-col. 2 line 39), Josel et al disclose it is advantageous to introduced a free positive or/and negative charge carriers into the linker which links the reactive coupling group of the metal complex to one of the ligands because it reduces the adsorption of conjugates of these complexes with an immunologically reactive substance and thus also improves the stability and recovery of the conjugates in immunoassays. Moreover an increased quantum yield can be achieved (col. 1 lines 44-52). Josel teach the electrochemiluminescence assays are carried out

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in the presence of a solid phase which is preferably composed of microparticles and in particular of magnetic microparticles which are provided with a reactive coating e.g. with streptavidin. In this manner immune or hybridization complexes containing a metal complex as a marker group can be detected bound to a solid phase ("metal complex used as a conjugate with a detection reagent" and "carried out as a heterogenous test") (col. 8 lines 1-15). It is desirable to include the electrochemiluminescence metal complex on solid phase by a reactive coating because it allows the assay reactants to be held in place by a magnet and released after the assay.

Therefore it would have been obvious to one of ordinary skill in the art as motivated by Josel et al to combine a charged linker to the metal complex of Fiaccabrino/Rubenstein in order to reduce the adsorption of conjugates of these complexes with an immunologically reactive substance and improve the stability and recovery of the conjugates in immunoassays so that an increased quantum yield can be achieved.

Therefore, it would have been obvious to one of ordinary skill in the art to substitute the ruthenium reagents of Fiaccabrino/Rubenstein with the metal complex and streptavidin coated magnetic microparticles of Josel because it allows the assay reactants to be held in place by a magnet and released after the assay.

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5. Claims 23, 26, 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar et al (US 2004/0090168 and provisional application 60/390816) in view of Welk (CA 2313144 A1).

Regarding claims 23, 26-28, Kumar teaches an apparatus for detecting an analyte in a sample using a luminescent metal complex, such as Ru(II)(bpy)<sub>3</sub> substituted with functional groups that are used for linking the label to biomolecules (Pg. 14 lines 18-24), as a labelling group, comprising (i) an electrode capable of oxidizing the metal complex an applied potential of 1.0-1.8V vs. Ag/AgCl (Pg. 16 lines 4-18), ("means for oxidizing the metal complex") and (ii) the electrode capable of introducing hydrogen gas by applying a -1.5 V ("means for generating nascent hydrogen") (Pg. 17 lines 1-11); and (iii) a light detector ("means for detecting chemiluminescence") (pg. 7 lines 1-7 and 17 lines 18-24). Kumar teaches the oxidation and reduction potentials are alternated (Pg. 17 line 10) and the electrodes can be positioned in separate regions (Figure 2A-2J). Kumar is silent about the oxidation and generation of nascent hydrogen take place in two separate reaction chambers.

Welk teaches an electrolytic cell for the generation of nascent hydrogen and oxidizing agents wherein there are separate chambers for the positive and negative electrodes (abstract). It is desirable to keep the oxidation and reduction chambers separate in order to make sure the oxidizing agents do not react with the reducing agents and the metals are completely oxidized before being reduced.



Therefore it would have been obvious to one of ordinary skill in the art to modify the method and device of Kumar with the separate oxidation and reduction chambers of Welk in order to to make sure the oxidizing agents do not react with the reducing agents and the metals are completely oxidized before being reduced.

Regarding claim 29, Kumar/Welk teach the electrodes come into contact with the metal complex. Regarding the “so that the nascent hydrogen will be formed within 50nm of the oxidized metal complex” is considered process or intended use limitations, which do not further delineate the structure of the claimed apparatus from that of the prior art. Since these claims are drawn to an apparatus statutory class of invention, it is the structural limitations of the apparatus, as recited in the claims, which are considered in determining the patentability of the apparatus itself. These recited process or intended use limitations are accorded no patentable weight to an apparatus. Process limitations do not add patentability to a structure, which is not distinguished from the prior art. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967); and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). The Courts have held that it is well settled that the recitation of a new intended use, for an old product, does not make a claim to that old product patentable. See *In re Schreiber*, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431

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(Fed. Cir. 1997). The Courts have held that the manner of operating an apparatus does not differentiate an apparatus claim from the prior art, if the prior art apparatus teaches all of the structural limitations of the claim. See *Ex Parte Masham*, 2 USPQ2d 1647 (BPAI 1987) (see MPEP § 2114).

6. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar et al (US 2004/0090168 and provisional application 60/390816) in view of Welk (CA 2313144 A1) and further in view of Bard et al (USP 5,714,089).

Regarding claim 25, Kumar et al teach the oxidation of the metal complex electrochemically using electrodes but is silent about the metal complex is oxidized chemically by PbO<sub>2</sub>, permanganate, Cer<sup>4+</sup> compounds or/and peroxodisulfate.

Bard et al teach that Ru(bpy)<sub>3</sub> can be oxidized by either chemically by PbO<sub>2</sub> or Cer<sup>4+</sup> compounds or electrochemically. (col. 4 lines 31-48). It is known that these are equivalent methods for oxidizing the metal complex in electrochemiluminescence.

Therefore it would have been obvious to one of ordinary skill in the art as motivated by Bard et al to oxidize the metal complex of Kumar et al with PbO<sub>2</sub> or Cer<sup>4+</sup> compounds because they are known as equivalent methods to oxidize the metal complex in electrochemiluminescence assays.

***Allowable Subject Matter***

7. Claims 18-20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. The following is a statement of reasons for the indication of allowable subject matter: The method of luminescent material wherein the reducing the metal complex by nascent hydrogen, wherein the nascent hydrogen is chemically generated by Li/butanol/H<sub>2</sub>SO<sub>4</sub>, Zn-Cu/ethanol or Zn/HCl or by ultrasound is not taught or fairly suggested because the prior art of record teach away from producing nascent hydrogen during electrochemiluminescence.

***Response to Arguments***

9. Claim rejection under 35 U.S.C. § 112, second paragraph have been withdrawn in view of the claim amendments.

10. Applicant's arguments with respect to claims 1-17, 21-23, 25-29 have been considered but are moot in view of the new ground(s) of rejection.

11. Applicant's arguments filed 1/28/2009 have been fully considered but they are not persuasive. Regarding claims 23, 25-26 and 28, Applicants argue that Kumar does not teach all of the limitations of the device, specifically that the means for oxidizing and the means for generating nascent hydrogen comprise two separate reaction chambers. There is no teaching, suggestion, or motivation in Kumar for the use of such separate means for oxidizing and the means for generating nascent hydrogen. It is noted that the electrodes of Kumar are fully capable of oxidizing and reducing (thus producing nascent hydrogen in the

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cleaning process) and therefore the structural limitations are met by Kumar.

Welk teach the limitation of the oxidizing and reducing electrodes in separate reaction chambers.

### ***Conclusion***

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**.

See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DENNIS M. WHITE whose telephone number is (571)270-3747. The examiner can normally be reached on Monday-Thursday, EST 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax

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phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lyle A Alexander/  
Primary Examiner, Art Unit 1797

/dmw/